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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/052,803	11/07/2001	Fernand Labrie	P/1259-637	3989

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OSTROLENK FABER GERB & SOFFEN
1180 AVENUE OF THE AMERICAS
NEW YORK, NY 100368403

EXAMINER	
JIANG, SHAOJIA A	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 02/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/052,803	LABRIE, FERNAND	
	Examiner	Art Unit	
	Shaojia A. Jiang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,13-19,22-24,35-41 and 44* is/are pending in the application.

4a) Of the above claim(s) *24 and 44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,13-19,22,23 and 35-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/1/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 1, 2004 has been entered.

This Office Action is a response to Applicant's request for continued examination (RCE) filed November 1, 2004, and response to the Final Office Action (mailed April 30, 2004), filed November 1, 2004 wherein claims 1-2, 13-19, and 22-23 have been amended; claims 3-12, 20-21, 25-34 and 42-43 are cancelled; claim 44 is newly submitted.

Currently, claims 1-2, 13-19, 22-24, 35-41 and 44 are pending in this application.

It is noted that claim 24 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected species, of record in the previous Office Action dated April 30, 2004. Note that new claim 44 is also directed to a non-elected species, same as claim 24. Thus, claim 44 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b).

Note that Applicant's election without traverse of the species of EM-652.HCl in claim 17 for the SERM compound, 17β-estradiol in claim 20 for as an estrogen, and

dehydroepiandrosterone (DHEA) for additional agent in claim 2, submitted April 30, 2002 has been recorded in the previous Office Action May 21, 2002.

Claims 1-2, 13-19, 22-23, and 35-41 are currently under examination on the merits.

Applicant's amendment amending claims 1-2, 13-19, and 22-23, filed November 1, 2004 with respect to the rejection made under 35 U.S.C. 112 first paragraph for lack of scope of enablement of record stated in the Office Action dated April 30, 2004 has been fully considered and is found persuasive to remove the rejection since the particular selective estrogen receptor modulator (SERM) compounds and estrogens have been recited. Therefore, the said rejection is withdrawn.

Claim Objection

Claim 35 is objected to under 37 CFR 1.75(c), as being of an improper dependent claim since claim 35 is dependent from claim 34 which has been cancelled. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2 and 22-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitations, "derivative" and "derivatives", "a prodrug of any of the forgoing additional agents" in the claims render claims 1-2 and 22-23 indefinite. The recitations, "derivative" and "derivatives" "a prodrug of any of the forgoing additional agents" are not clearly defined in the specification. Hence, one of ordinary skill in the art could not interpret the metes and bounds as to these recitations in the claims, since one of ordinary skill in the art would clearly recognize that many widely varying groups could possibly substituting the compounds herein would read on the "pro-drug, derivative or derivatives " of the compounds.

Given the fact that any significant structural variation to a compound would be reasonably expected to alter its properties, e.g., physical, chemical, physiological effects and functions. Thus, it is unclear and indefinite as to the "pro-drug, metabolite, analogue, derivative" of compounds herein encompassed thereby.

Therefore, the scope of claim is indefinite as to the composition encompassed thereby.

Claims 1 and 22 contain the abbreviation or trademark/trade name "DES". Where a trademark or trade or abbreviation name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the abbreviation or

trademark or trade name cannot be used properly to identify any particular material or product. A abbreviation or trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a abbreviation or trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the abbreviation is used to identify/describe particular agent, accordingly, the identification/description is indefinite.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 and 22 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 10 of U.S. Patent No. 6,710,059.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent is drawn to a pharmaceutical composition comprising EM-652.HCl or EM-800 as the SERM compound, and an estrogen.

The claim of the instant application is drawn to a pharmaceutical composition comprising the same SERM compound such as EM-652.HCl or EM-800, and an estrogen such as 17β-estradiol.

Thus, the instant claim 1 is seen to be anticipated by claim 10 of U.S. Patent No. 6,710,059.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 13-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Simard et al. (International Journal of Cancer (1997), 73(1), 104-112, "83" in PTO-1449 submitted November 7, 2001).

Simard et al. discloses a composition comprising 17β-estradiol (E2), the instant estrogen, and a simultanoues incubation with EM-652 or EM-800, the instant SERM compound, and a pharmaceutical diluent or carrier such as water in vitro. See abstract, page 104-105; Fig 2-12 at page 106-111. Thus, the testing results show that EM-652 or EM-800 as non-steroidal antiestrogens are useful in treating breast cancer in patients (see abstract), particularly including those woman patients who need to take estrogens daily for hormone replacement therapy (HRT).

Thus, the disclosure of Simard et al. anticipates claims 1 and 13-16.

Claims 1-2 and 13-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Couillard et al. ("8" in PTO-1449 submitted November 1, 2004).

Couillard et al. discloses that administering estrone, the instant estrogen, to mice while co-administering EM-800 and DHEA in a composition with a pharmaceutical diluent or carrier, is useful in inhibiting breast tumors or cancer growth in mice. See the entire article.

Thus, the disclosure of Couillard et al. anticipates claims 1-2 and 13-16.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 17-19, 22-23, and 35-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Simard et al. or Couillard et al. as applied above.

The same disclosure of Simard et al. or Couillard et al. has been discussed in the 102(b) rejection set forth above.

The prior art does not expressly disclose the employment of a kit to store the compositions of Simard et al. or Couillard et al. The prior art does not expressly disclose the employment of the known pharmaceutically acceptable salt of the acid in a pharmaceutical composition or a kit.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ a kit for comprising the composition of Simard et al. or Couillard et al. and to employ the known pharmaceutically acceptable salt of the acid in a pharmaceutical composition or a kit, since the patient pack or kit and the pharmaceutically acceptable salts are all deemed obvious; they are all within the knowledge and conventional skills of pharmacologist to conveniently assist the user and prescriber for easy dispensary of the medication.

Claims 1-2, 13-19, 22-23, and 35-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Luo et al. ("54", PTO-1449 submitted November 7, 2001) and Barrett-Connor et al. ("4", PTO-1449 submitted November 7, 2001), and Do Nascimento (of record) in view of Labrie et al. (WO 96/26201, PTO-1449 submitted November 7, 2001), for the same reasons of record in the Office Action dated April 30, 2004.

Luo et al. discloses that an estrogen, DHEA alone, or the particular SERM (antiestrogen), EM-800 alone (having 2S configuration and moieties convertible in vivo to hydroxyl), is known to be useful in a method of treating hyperlipidemia by decreasing serum lipid levels such as triglyceride and cholesterol levels. See abstract and page 4436 Fig. 1 "Structure of EM-800", page 4438 the left column "Effect on serum lipid levels". Luo et al. further discloses that the combination of DHEA and EM-800 exerts more potent effect on reducing serum lipid levels than each compound used alone (page 4438 the left column "Effect on serum lipid levels" and page 4439 Fig. 4, and page 4443 the left column.

Barrett-Connor et al. teaches that SERMs are capable of lowering serum lipid levels to reduce the risk of coronary heart disease, as estrogen does. See abstract.

Do Nascimento teaches that the particular estrogen, 17β-estradiol, is useful in treating hypercholesterolemic patients (see abstract).

The prior art does not expressly disclose the employment of the combination of an estrogen such as 17β-estradiol and the particular SERM, EM-652.HCl, or further combining with DHEA in a pharmaceutical composition.

Labrie et al. (WO 96/26201) discloses that both EM-800 and EM-652 or EM-652.HCl are antiestrogens (SERMs), and EM-800 has moieties convertible in vivo to hydroxyl to become EM-652. Thus, EM-800 is a metabolite of EM-652, having the same functional property and activity.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ of the combination of an estrogen such as 17β-estradiol and the particular SERM, EM-652.HCl, or to further combine with DHEA, in a pharmaceutical composition.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ the combination of an estrogen such as 17β-estradiol and the particular SERM, EM-652.HCl, or to further combine with DHEA, in a pharmaceutical composition, since estrogens such as 17β-estradiol and DHEA are well known in the art to be used in methods of treating hyperlipidemia by decreasing serum lipid levels such as triglyceride and cholesterol levels according to the cited prior art herein. Moreover, the particular SERM, EM-800, a known metabolite of EM-652

(convertible in vivo to hydroxyl to become EM-652), alone or in combination with an estrogen such as DHEA, is known to be useful in a method of treating hyperlipidemia by decreasing serum lipid levels such as triglyceride and cholesterol levels according to Luo et al.

Therefore, one of ordinary skill in the art would have reasonably expected that combining an estrogen such as 17β-estradiol and the particular SERM, EM-652.HCl, or further combining with DHEA, all known useful for the same purpose, i.e., treating hypercholesterolemia, would improve the therapeutic effects for treating the same disorder, hypercholesterolemia, and/or would produce additive therapeutic effects in treating the same. See *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980) regarding combination inventions. It is considered prima facie obvious to combine two active composition components into a single composition to form a third composition useful for the very same purpose.

Further, the teachings of Luo et al. that the combination of DHEA and EM-800 exerts more potent effect on reducing serum lipid levels than each compound used alone clearly provides the motivation of the instant claimed method employing the combination of EM-652, 17β-estradiol and DHEA.

Furthermore, one of ordinary skill in the art would have been motivated to prepare a kit comprising the same composition because the preparation of a kin comprising a pharmaceutical composition is considered well in the competence level of an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art.

Thus the claimed invention as a whole is clearly prima facie obvious over the teachings of the prior art.

Applicant's remarks filed November 1, 2004 with respect to the rejection made under 35 U.S.C. 103(a) as being unpatentable over Luo et al. and Barrett-Connor et al. and Do Nascimento (of record) in view of Labrie et al. of record in the previous Office Action April 30, 2004 have been fully considered but are not deemed persuasive as to the nonobviousness of the claimed invention over the prior art as further discussed below.

The examiner notes that DHEA is not covered by estrogen as Applicant asserts in the remarks. However, claim 2 clearly recites DHEA, and claim 1 does not exclude additional, unrecited elements such as DHEA since the transitional phrase "comprising" is employed in the instant claimed composition. Applicant is requested to note that the transitional term "comprising" is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. See MPEP 2111.03.

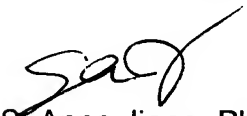
Thus, this rejection is maintained.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (571)272-0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



S. Anna Jiang, Ph.D.
Primary Examiner
Art Unit 1617
February 2, 2005